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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/980,395	11/28/97	SONTHEIMER	H	D5858D1

HM21/0805

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EXAMINER
SUN-HOFFMAN, L

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/05/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/980,395	Sontheimer et al
Examiner	**Group Art Unit**
Lin Sun-Hoffman	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-4 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-4 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-4 are pending for the examination. Claims 5-20 are canceled.

Specification

2. The headings of columns 6, 7 and 9 in Table V on page 45 are unclear in typing.

Correction is required.

Double Patenting

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process . . . may obtain a patent therefor . . . " (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 0/8980394. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 is drawn to a pharmaceutical composition comprising an antibody which recognizes an antigen that is glioma or meningioma specific chloride channel and a pharmaceutically acceptable carrier.

While the specification teaches an antibody specific to a fusion protein of GST-chlorotoxin (see page 53), it does not teach any antibody specific to glioma or meningioma chloride channel protein.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification fails to teach an antibody that specific to the chloride channel protein. The specification fails to teach how to obtain a chloride channel protein that is specific to glial-derived or meningioma-derived tumor cells and to make an antibody against it.

In consideration of the obtaining an antibody, it is often encountered in the art how to obtain an antigen, wherein the molecular weight of such an antigen is determined by different methods. The physical property of the chloride channel is not disclosed in the instant invention

wherein when a protein is recited it should include a molecular weight and the method by which it was determined, e.g., whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, whether the determination was made under denaturing or non-denaturing conditions and whether reducing or non-reducing conditions were used. Also it should include the method to isolate the chloride channel, the determination of the sequence and the structure of said protein. The method of making an antibody specific to glial-derived or meningioma-derived tumors cells should also be disclosed so that one of skill in the art can duplicate the claimed invention. Claiming an antibody and chloride channel by ambiguous physical characteristics and functional attribute fails to distinctly claim what a chloride channel protein is and what is the claimed antibody. Therefore, in view of the amount or direction or guidance presented, the absence of working examples, the predictability or unpredictability of the art with respect to making an antibody specific to glioma or meningioma chloride channel, it would require undue experimentation for one skilled in the art to practice to successfully obtain the claimed invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1-4 are drawn to a pharmaceutical composition comprising a ligand binding specifically to glial-derived or meningioma-derived tumor cells, wherein the ligand is either an antibody or chlorotoxin-like protein specifically recognizing an antigen in chloride channels of glial-derived tumor cells.

The specification does not set forth sufficient teachings to allow one skilled in the art to apply the claimed pharmaceutical compositions. The specification does not provide teachings to establish effective dosages or methods of administration of compositions specific for glioma or meningioma. No working examples are provided which would provide sufficient guidance to allow one skilled in the art to practice the above embodiments of the invention with a reasonable expectation of success.

While the specification teaches that an immunotoxin can kill glioma cells in vitro, characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Further, an anti-tumor agent must accomplish several tasks to be effective. It must be delivered into the circulation, to cross the blood-brain barrier to supply the tumor, to interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. In addition the target cell must not have an alternate means of survival despite action at the proper site for the drug. In vitro assays cannot duplicate the complex conditions of in vivo therapy. In the assays, composition is in contact with cells during the entire exposure period. This is not the case in vivo, where exposure of the target site may be delayed or inadequate. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The composition may be inactivated in vivo before producing a sufficient effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life of the protein and the in vitro tests of record do not sufficiently duplicate the conditions which occur in vivo. In addition, the composition may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity

is to be exerted, may be absorbed by fluids, cells and tissues where the composition has no effect, circulation into the target area may be insufficient to carry the composition and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art. No evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 are vague and indefinite in reciting a chlorotoxin-like protein. The definition of chlorotoxin-like protein lacks metes and bounds.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

10. (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 3 are rejected under 35 U.S.C. 102(a) as being anticipated by Ullrich et al (NeuroReport, 7, 1020-1024, April 10, 1996).

Ullrich et al teach a pharmaceutical composition chlorotoxin that binds to glial-derived or meningioma-derived tumor cells (see page 1022, column 1, paragraph 3; and page 1021, Table 1).

Nakamura et al teach an monoclonal antibodies to glial-derived tumor cells. (See abstract and page 1511, Introduction, first paragraph).

12. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Phillips et al (Cancer Research, 54, 1008-1015, 1994)

Phillips et al teach treatment of glioblastoma with a pharmaceutical composition of TGF-alpha that specifically binds to glial-derived cells (see abstract, page 1009, column 2, paragraph 3; and page 1010, column 2, Table 1).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1, 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeBin et al (Am. J. Physiol. 264/2, 33-2 (C361-C369), 1993) or Malinowska et al (13th Annual Meeting of